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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/147,947	03/24/1999	NOBUO TSURUOKA	001560-349	2472

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EXAMINER	
MOORE, WILLIAM W	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 09/06/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/147,947	TSURUOKA ET AL.	
	Examiner	Art Unit	
	William W. Moore	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-9,12,14-16 and 21-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *21* is/are allowed.

6)☒ Claim(s) *5-9,12,14-16 and 22-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Prosecution Application

The request for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/147,947, Paper No. 20 filed on July 1, 2002, is acceptable and a CPA has been established. An action on the CPA follows on claims 5-9, 12, 14-16 and 21-59 as amended in Paper No. 17, Amendment E filed November 30, 2001. Amendments to claims 5, 6, 14-16 and 21 submitted in Amendment E inserting the term "isolated" overcome the rejection of record under 35 U.S.C. §101 set forth in Paper No. 14 mailed June 1, 2001, and the amendments to claims 5, 6, 14-16 and 21-30 deleting the term, "or its partial peptide", submitted in Amendment E overcome the rejections of claims herein over the prior art of record. Thus claim 21 is indicated to be allowable herein and claims 22-24 describing specific, disclosed, serine protease domains are subject only to rejections herein under the second paragraph of 35 U.S.C. §112.

Claim Objections

Claims 6, 9, 27-30, 45-50 and 54-59 are objected to because of the following informalities: Substandard grammar mars each of these claims. Appropriate correction of claims 6, 9, 27-30 and 45-50 by inserting the definite article, "the", or the indefinite article, "a" or "an", before each noun in each claim lacking the proper use of an article is required. It is noted that several claims will require insertions of articles before two or more nouns. Correcting each of claims 54-59 by inserting "is" before each occurrence of the word "prepared" is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6, 8, 12, 27-30, 34-36, 40-44, 47-50, 52, 53, and 55-59 are rejected, essentially for reasons of record, under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 44 remains rejected for reasons of record set forth at pages 2-4 of Paper No. 14 in view of its recitation of "or their partial peptides". The claim amendments of Paper No. 17 do not cancel any of claims 6, 12, 27-30, 34-36, 40-43, 47-50 and 55-59 subject to the rejection of record, and among the enumeration of claims at line 30 of page 2 of Paper No. 14, because they recite, or depend from claims reciting, is hybridizable with DNA that codes for the [protease or domain] as claimed in claim 21 [or 22, or 23, or 24], under stringent conditions". There is no disclosure, explicit or inherent, in the specification of such "hybridizable" DNAs that need not encode the neurotrypsin protease of SEQ ID NO:6, or its protease domain having the amino sequence from position 578 through position 822 of SEQ ID NO:6, or a kringle domain of the protease having the amino sequence from position 40 through position 112 of SEQ ID NO:6, or one of the four scavenger receptor cysteine-rich domains of the protease selected from the group consisting of an amino acid sequence from position 117 through position 217 of SEQ ID NO:6, an amino acid sequence from position 227 through position 327 of SEQ ID NO:6, an amino acid sequence from position 334 through position 433 of SEQ ID NO:6, and position 447 through position 547 of SEQ ID NO:6. There is no teaching of the design or preparation of hybridizable DNAs encoding divergent amino acid sequences, nor is there any evidence of the identification of hybridizable DNAs encoding divergent amino acid sequences in other sources. Such hybridizable DNAs, and whatever divergent, undisclosed, amino acid sequences they encode, include DNAs encoding, and encoded amino acid sequences of, the "partial peptides" deleted from claims 5, 6, 9, 12, 15, 16, 21-30 and 45-59, as well as the "partial peptides" not yet deleted from claim 44.

Claim 8 is rejected because its recitation "[a] host transformed by the expression vector" embraces all kinds of hosts, including transgenic animals and transgenic plants, but the specification discloses no more than host cells transformed with an expression vector. Neither does the specification otherwise provide any inherent support for a transgenic animal or plant transformed with an expression vector comprising a DNA encoding all or part of the neurotrypsin protease of SEQ ID NO:6 by disclosing, e.g., the preparation of a suitable vector or the transfection or transformation of a multicellular organism with any expression vector.

Claims 52, 53, 55, 56 58 and 59 are also rejected because they describe processes comprising measuring inhibitory or activating activity of substances contacted with domains for which the specification neither discloses, teaches, nor suggests any measure of activity. Only the disclosure of an assay suitable for measuring the proteolytic activity of the human neurotrypsin at page 26 of the specification offers inherent support for the assay methods recited by claims 51 and 54. The specification does not otherwise disclose or suggest the nature or source of measuring assays that support the limitations of claims 52, 53, 55, 56 58 and 59. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. §112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). No relevant identifying characteristics of "hybridizable DNAs" are present in the specification, nor any suggestion how to measure "activity" of kringle domains or scavenger receptor cysteine-rich domains.

The Court of Appeals for the Federal Circuit has determined that a claimed invention must be described with such "relevant identifying characteristic[s]" that the public could know that the inventor possessed the invention at the time an application for patent was filed, rather than by a mere "result that one might achieve if one had made that

invention". *University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The specification's treatment of subject matters of claims 6, 12, 27-30, 34-36, 40-44, 47-50, 52, 53, and 55-59 is entirely prospective and skilled artisans in the relevant fields of molecular biology and mammalian genetics could neither predict the structure, or the coding capacities, of "hybridizable DNAs that might support practice of the invention of these claims, nor predict the conditions necessary to measure inhibitory or activating activity of substances contacted with kringle domains or scavenger receptor cysteine-rich domains. The rejection of record is sustained.

Claims 6, 12, 27-30, 34-36, 40-44, 47-50, 52, 53, and 55-59 remain rejected for reasons of record under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for

(a) preparation of a human neurotrypsin of claim 21 consisting of the amino acid sequence of SEQ ID NO:6 and a nucleotide sequence encoding it,

(b) preparation of a serine protease domain of a human neurotrypsin of claim 22 comprising the amino acid sequence region from position 578 to position 822, inclusive, of SEQ ID NO:6 and a nucleotide sequence encoding it,

(c) preparation of a kringle domain of a human neurotrypsin of claim 23 comprising the amino acid sequence region from position 40 to position 112, inclusive, of SEQ ID NO:6 and a nucleotide sequence encoding it,

(d) preparation of a scavenger receptor cysteine-rich domain of a human neurotrypsin of claim 24 comprising an amino acid sequence region selected from the group of regions consisting of position 117 to position 217, inclusive, of SEQ ID NO:6, position 227 to position 327, inclusive, of SEQ ID NO:6, position 334-433, inclusive, of SEQ ID NO:6, **and** position 447 to position 547, inclusive, of SEQ ID NO:6, as well as nucleotide sequences encoding each, and,

(e) methods utilizing either the human neurotrypsin of SEQ ID NO:6 of claim 21 or its serine protease domain of claim 22 in processes for screening physiologically active substances that have some certain, recognizable, result,

does not reasonably provide enablement for the preparation of the myriad of "hybridizable DNAs" that do not encode SEQ ID NO:6 or one of its specific domains, or for the divergent, encoded products of such "hybridizable DNAs" or for the use of the specific kringle domain or scavenger receptor cysteine-rich domains of SEQ ID NO:6 in processes for screening physiologically active substances that have some certain, recognizable, result. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The recitations of the claims that describe "hybridizable DNAs" reach nucleic acid sequences encoding polypeptides, and encoded polypeptide products, wherein any number

of amino acid insertions, deletions, or substitutions may occur in the amino acid sequence of SEQ ID NO:6 and its specific domains. The specification does not enable the design or preparation of such "hybridizable DNAs" because it fails to teach any specific locations for substitutions, deletions or insertions of amino acids anywhere in the amino acid sequence of SEQ ID NO:6, and teaches no substituents, that will predictably permit the protease, or its several domains, to function. The specification provides no guidance for the practice of assays that might somehow measure "an activity" of either the kringle domain or the scavenger receptor cysteine-rich domains of SEQ ID NO:6 in any process for screening physiologically active substances to obtain a useful result.

As noted in the rejection of record, the CCPA, the predecessor of the present Court of Appeals for the Federal Circuit, which held that "mak[ing] and screen[ing]" any and all possible alterations cannot be considered enabling because a reasonable correlation must exist between the scope of guidance provided by the specification and the scope asserted in the claimed subject matter. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 25 (CCPA 1970) (scope of enablement varies inversely with the degree of unpredictability of factors involved in physiological activity of small peptide hormone); see also, *Ex parte Maizel*, 27 USPQ2d 1662, 1665 (Bd. Pat. App. & Int. 1992) (functional equivalency of divergent gene products not supported by disclosure only of a single B-cell growth factor allele). The instant specification provides no guidance whatsoever for amino acid sequence alterations, thus the rejection of record is sustained.

Claim 44 is for reasons or record rejected, and claims 5-9, 12, 14-16 and 22-59 are rejected, under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 44 remains rejected reasons or record for its recitation of "or their partial peptides" because this phrase describes a narrow range or limitation that falls within the broad range or limitation, the protease domain amino acid sequence of claim 44, in the

same claim, failing to clearly set forth the metes and bounds of the desired subject matter. Deleting the term, "or their partial peptides", will overcome this aspect of the rejection.

Claims 22-24 are indefinite in reciting "indicated in SEQ ID NO:6" in making reference to specific regions of the amino acid sequence of SEQ ID NO:6 because neither SEQ ID NO:6 as it is set forth in the Sequence Disclosure, nor any other part of the Sequence Disclosure, indicates anything. They merely represent information. Substituting the simple preposition, "of", for each occurrence of "indicated in" will overcome this aspect of the rejection.

Claim 24 is independently indefinite in its improper statement of a Markush group, thus failing to define the boundaries of the intended members of the Group. Replacing the only occurrence of "or" in claim 24 with "and" will overcome this aspect of the rejection.

Claims 5, 6, 9, 14, 15, 16, 25, 26, 27, 54, 55 and 56 are indefinite in reciting "or domain" because claims 21-24 from which they ultimately depend describe either an integral protease, as in claim 21, or a specific domain: a serine protease domain in claim 22, a serine protease kringle domain in claim 23, or a receptor scavenger cysteine-rich domain in claim 25. No independent claim save claim 25 describes alternative products. Thus there is no basis in logic, nor an antecedent basis, for reciting the disjunctive term "or domain" in any of the dependent claims. This aspect of the rejection may be overcome by i) deleting the phrase "or domain" wherever it occurs, ii) amending each claim that depends from claim 21 to recite "the serine protease", and, iii) amending each claim that depends from one of claims 22, 23, or 24 to recite the specific domain intended.

Claims 15, 16, 23, 24, 28-30, 44-46 and 48-59 are independently indefinite in the nonspecific recitations of "domain" in each claim. This is because claims 23 and 24 fail to designate the particular source, a serine protease, of the specific domains they recite, and because claims 15, 16, 28-30, 44-46 and 48-59 which they ultimately depend from

claims 22, 23 and 24 fail to describe the specific nature of any domain they recite, e.g., **a serine protease domain** in those claims which depend from claim 22, **a serine protease kringle domain** in those claims which depend from claim 23, and **a receptor scavenger cysteine-rich domain** in those claims which depend from claim 25. Inserting the specific designation of the intended domain before each occurrence of the word domain in claims 15, 16, 23, 24, 28-30, 44-46 and 48-59 will overcome this aspect of the rejection.

Claims 7, 8, 12, 31-43 and 47 are included in this rejection because they depend from one of more of claims 5, 6 and 22-24 rejected herein yet fail to resolve the indefinite description of the claim from which they depend.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 703.308.0583. The examiner can normally be reached from 8:00AM-6:30PM EST on Mondays, Wednesdays, and Fridays and from 11:30AM-6:00PM EST on Tuesdays and Thursdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached at 703.308.3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703.308.4242 for regular communications and 703.308.0294 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703.308.0196.

William W. Moore
September 5, 2002

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